ORIGINAL ARTICLE

A Study on Assessment of Liver Functions among Patients with Rat Killer Paste Poisoning

Suganthi R [1], Manoj J [2]
[1]Senior Resident,[2]Junior Resident in Govt Thiruvarur Medical college

ABSTRACT
BACKGROUND AND OBJECTIVES: Yellow phosphorous, a toxic rodenticide which is readily and widely used as rodenticide. Many times, ingestion of yellow phosphorous either intentionally or accidentally results in mortality due to its hepatotoxic property. Thus this study was done to assess the acute liver injury that occurs secondary to rat killer paste poisoning. **METHODS:** This observational study was conducted at Thiruvarur medical college, Thiruvarur. Total of 60 patients, who presented with history of ingesting rat killer paste during the study period of January 2016 to July 2016 were included in the study. After taking informed consent, complete history was taken and Liver Function Test (LFT) were done on day 1, day 3 and day 5 for who got admitted with history of ingesting rat killer paste. **RESULTS:** Among the 60 patients, 22(36.7%) patients were died and the rest 38(63.3%) patients were discharged. On day 1 of liver function test, the bilirubin and liver enzymes were elevated nut on subsequent assessment of liver function on day 3 and day 5, all parameters like bilirubin, SGOT, SGPT, PT and INR were improved comparatively on day 3 and day 5 than day 1, which was also found to be statistically significant. **CONCLUSION:** Acute yellow phosphorus poisoning can result in impairment of liver function test which is comparably highly altered during first stage of intoxication and subsequently better during second and third stage and that could be due to supportive treatment.
Keywords: Rat Killer Paste, Yellow Phosphorous, Liver Function Test

INTRODUCTION

Elemental phosphorous commonly present in two forms, namely, red phosphorous and yellow phosphorous. Red phosphorous is insoluble and completely unabsorbable and thus it is non-toxic whereas, yellow phosphorous, which is also referred as white phosphorous, a commonly used rodentiocide, has soluble property and thus gets easily absorbed and causes damage to hepatic, gastrointestinal, renal and cardiovascular systems. This toxic rodenticide is available as both powder and paste forms containing 2%-5% of yellow phosphorous. It has been also used in fertilizerindustry, military ammunition and in firecrackers.

Corresponding Author:
Dr. Suganthi R
No 8, Cauvery Nagar,
Dr Moorthyroad ,
Kumbakonam 612001 ,
Thanjavur District, Tamilnadu
Contact No: 9443070613
Email: drrsuganthi@gmail.com

Other rat poisons that are commonly used are zinc phosphide, aluminum phosphide and warfarin but among these chemicals yellow phosphorus has received less attention as a constituent of rat poisons. In the developing country like India, poisoningcommonly results from ingestion of rodenticide pastes were, withsuicidal intention. Also it was reported that case fatality rate is as high as 20–50%, has been reported in severe cases.[1] Complications, that occurs due to ingestion of yellow phosphorous includes acute toxic hepatitis with or without liver failure, renal failure, encephalopathy, cardiac arrhythmias, profound cardiogenic shock, coagulopathy and bleeding.[2] Extensive skin burns and systemic toxicity may result from yellow phosphorus explosions.[3] Severe intoxications were characterized by multisystem organ failure which usually results in mortality.[4] The lethal dose after oral ingestion of white phosphorus is 1 mg/kg of body weight, al- though small amounts as little as 15 mg have resulted in

death.[5] Among the complications, the most common complication reported was liver failure, which occurs secondary to yellow phosphorous intoxication6. Thus this study was conducted in order to find the exact sequence of acute liver injury that occur secondary to ingestion of yellow phosphorous.

MATERIALS AND METHODS

This hospital based observational study was conducted at Thiruvarurmedical college, Thiruvarur. Ethical committee clearance was obtained before commencing the study. Informed consent was obtained either from patients or from their relatives. If patient was conscious or as soon as they recover, consent was taken from patients also. There were 78 patients presented with alleged history of ingesting rat killer paste in the emergency medical ward during the study period of January 2016 to July 2016. Among them 18 patients, who gave history of jaundice and infections that cause liver injury in the past 2 months, suffering from serious systemic diseases, patient consumed other than rat killer paste like rat killer powder and biscuit and patients on hepato toxic drugs were excluded from the study and 60 patients were chosen as study subjects. Complete history was taken during the time of admission and Liver Function Test (LFT) were done on day 1, day 3 and day 5, for all the 60 patients, who got admitted in emergency medical ward with history of ingesting rat killer paste compound.All patients were managed with usual decontamination methods including nasogastric lavage and treated immediately. Patients are treated with intramuscular vitamin k, proton pump inhibitors and laxatives. Injection N – Acetyl cysteine /T.N- Acetyl cysteine was given according to the schedule. Counseling was given to the survivors and autopsy was done for all expired cases.Data were analyzed using SPSS 16 and appropriate statistical test like Chi square test and one way ANOVA ‘f’ test were used in this study.

OBSERVATIONS

Among 78 patients, 18 patients were excluded as they were not fulfilling the criteria and the rest 60 patients were included for analysis and among them 22(36.7%) patients were died and the rest 38(63.3%) patients were discharged. For all the 60 patients, liver function test were done on day1, 3 and 5. During day 1 of liver function test, among the patients discharged and died there were 17 (45.5%) and 10 (44.7%) patients respectively were reported with jaundice. With elevated SGOT of more than 100 there were 7(31.8%) patients who died and 8(21.1%) patients who were discharged. Similarly, with elevated SGPT of more than 100 there were 7(31.8%) patients who died and 5(13.2%) patients who were discharged. Also among the patients discharged and died there were 1 (2.5%) and 1(4.5%) patients respectively were reported with INR more than 3 (Table 1).

Table 1: Day 1 – Liver Function Test (LFT) and outcome of rat killer paste poisoning

Parameters	Guideline values	No. of patients Died (%)	No. of patients Discharged (%)
BILIRUBIN	Below1.3 mg/dl	12 (54.5)	21 (55.3)
	1.3 – 3 mg/dl	3 (13.6)	10 (26.3)
	3 – 5 mg/dl	6 (27.35)	5 (13.2)
	Above 5 mg/dl	1 (4.5)	2 (5.3)
SGOT	Below 100units/l	15 (68.2)	30 (78.9)
	100 – 500 units/l	6 (27.3)	8 (21.1)
	More than 500 units/l	1 (4.5)	0
SGPT	Below 100 units/l	15 (68.2)	33 (86.8)
	100 – 500 units/l	6 (27.3)	5 (13.2)
	More than 500 units/l	1 (4.5)	0
PT	Below 15 sec	14 (63.6)	22 (57.9)
	15 – 25 sec	7 (31.8)	15 (39.5)
	Above 25 sec	1 (4.5)	1 (2.6)
INR	Below 3	21 (95.5)	37 (97.4)
	3 – 5	1 (4.5)	1 (2.6)

During day 3 of liver function test, among the patients discharged and died there were 17 (45.5%) and 10 (44.7%) patients respectively were reported with serum bilirubin more than 1.3mg/dl. With elevated SGOT of more than 100 there

were 7(31.8%) patients who died and 8(21.1%) patients who were discharged. Similarly, with elevated SGPT of more than 100 there were 7(31.8%) patients who died and 5(13.2%) patients who were discharged. With respect to elevated PT more than 15, there were 8 (36.3%) patients and 20 (52.6%) patients were died and discharged, respectively. Also among the patients discharged there were 1 (2.5%) patients reported with INR more than 3 and among the patients died all of them had INR below 3 during day 3. Also there was a significant association reported between the serum bilirubin levels, SGOT, SGPT, PT and INR levels with the outcome of rat killer paste poisoning on Day 3 (Table 2).

Table 2: Day 3 – Liver Function Test (LFT) and outcome of rat killer paste poisoning

Parameters	Guideline values	No. of patients Died (%)	No. of patients Discharged (%)	p value
Bilirubin	Below1.3 mg/dl	12 (54.5)	21 (55.3)	.014*
	1.3 – 3 mg/dl	3 (13.6)	10 (26.3)	
	3 – 5 mg/dl	6 (27.3)	5 (13.2)	
	Above 5 mg/dl	1 (4.5)	2 (5.3)	
SGOT	Below 100 units/l	15 (68.2)	30 (78.9)	.021*
	100 – 500 units/l	6 (27.3)	8 (21.1)	
	More than500 units/l	1 (4.5)	0	
SGPT	Below 100 units/l	15 (68.2)	33 (86.8)	.016*
	100 – 500 units/l	6 (27.3)	5 (13.2)	
	More than500 units/l	1 (4.5)	0	
PT	Below 15 sec	17 (63.6)	18 (47.4)	.013*
	15 – 25 sec	7 (31.8)	19 (50)	
	Above 25 sec	1 (4.5)	1 (2.6)	
INR	Below 3	22 (100)	37 (97.4)	.003*
	3 – 5	0	1 (2.6)	

During day 5 of liver function test, among the patients discharged and died there were 7 (18.4%) and 4(18.2%) patients respectively were reported with serum bilirubin more than 1.3mg/dl. With elevated SGOT of more than 100 there were 3(13.6%) patients who died and 6 (15.8%) patients who were discharged. Similarly, with elevated SGPT of more than 100 there were 3(13.6%) patients who died and 3 (7.9%) patients who were discharged. With respect to elevated PT more than 15, there were 4 (18.1%) patients and 8 (21.1%) patients were died and discharged, respectively. All the patients, who were discharged and died, reported INR below 3 during day 5. Also there was a significant association reported between liver function test parameters like serum bilirubin levels, SGOT, SGPT and PT levels with the outcome of rat killer paste poisoning on Day 5 (Table 3).

Table 3: Day 5 – Liver Function Test (LFT) and outcome of rat killer paste poisoning

Parameters	Guideline values	No. of patients Died (%)	No. of patients Discharged (%)	p value
Bilirubin	Below1.3 mg/dl	18 (81.8)	31 (81.6)	.007*
	1.3 – 3 mg/dl	1 (4.5)	3 (7.9)	
	3 – 5 mg/dl	1 (4.5)	2 (5.3)	
	Above 5 mg/dl	2 (9.1)	2 (5.3)	
SGOT	Below 100 units/l	19 (86.4)	32 (84.2)	.017*
	100 – 500 units/l	3 (13.6)	5 (13.2)	
	More than500 units/l	0	1 (2.6)	
SGPT	Below 100 units/l	19 (86.4)	35 (92.1)	.006*
	100 – 500 units/l	3 (13.6)	2 (5.3)	
	More than 500 units/l	0	1 (2.6)	
PT	Below 15 sec	18 (81.8)	30 (78.9)	.014*
	15 – 25 sec	3 (13.6)	8 (21.1)	
	Above 25 sec	1 (4.5)	0	
INR	Below 3	22 (100)	38 (100)	

Out of 60 patients, 22 (36.7%) patients were died and among them there were 12 (54.5%) cases, who were died of hepatic encephalopathy followed by myocarditid

and coagulopathy in 11(50%) and 9 (40.9%) cases respectively.

DISCUSSION

Yellow phosphorous produces hepatotoxicity in a dose dependent manner[7]. In majority of the patients, amino transferase was reported mostly begin to rise within one day of exposure. Time of enzyme peak and level rise differ significantly between patient who survives and who dies. Patients, who die have average peak of sixteen times of normal, reached in 2-3 days. In those who survive, alanine aminotransferase (SGOT) raises eight times normal, reaching peak in six days. Coagulopathy is seen in 20 %[6] of patients. Serum triglyceride levels fall as toxicity develops, there may also be increase in serum and urinary ketones. It consumes oxygen in liver cells, is a protoplasmic poison which uncouples oxidative phosphorylation, in turn leading to decrease in intrahepatocyte ATP levels[8]. It also affects transition of triglyceride as betalipoproteins. Massive hepatic steatosis is a hallmark of white phosphorus toxicity with rise in triglyceride level in two hours, peaking in two days. Hepatic necrosis particularly occurs in zone 1, distinct from acetaminophen and carbon tetrachloride, hepatic glycogen are decreased due to increased glucose-6- phosphatase activity. A non specific finding of huge increase in rough endoplasmic reticulum, is typically found in this poison[9,10]. Liver biopsy showed signs of acute hepatocellular necrosis and also shows fibrosis and piecemeal necrosis. Investigations like serial monitoring of liver function tests like serum Bilurubin, SGPT, SGOT, prothrombin time and INR are must. Patients were treated with Liver protective agent like N-Acetyl cysteine and Liver supportives like dextrose containing solutions and ursodeoxycholic acid. Clinically, patients who consumed, yellow phosphorous undergo three stages. During first stage of intoxication, patients usually present with either mild gastro intestinal the mortality, occurring due to rat killer paste poisoning. symptoms or asymptomatic and this occurs with 24 hours of ingestion of phosphorous. The second stage of intoxication, which occurs between 24 to 72 hours after ingestion, patients will be symptoms free and may be even discharged prematurely. During this stage, there may be slight elevation in the liver function test. Third stage, which occurs 72 hours after ingestion, during which the symptoms usually resolves or death occurs[11].Patients may present with acute hepatic failure, coagulopathy, and deranged liver function, as reported in this study, which is comparable with the study done by Fernandez et al[6] and also they reported liver histology at this stage may show steatohepatitis and necrosis. Fernandez et al[6] in a series of 15 patients have reported a mortality of 27%, confirming that yellow phosphorus is extremely lethal when ingested. At times, few patients may develop acute tubular necrosis and present with acute renal failure. Central nervous system effects include changes in mental status like confusion, psychosis, hallucinations, and coma. Cardiac toxicity includes hypotension, tachycardia, arrhythmias, and cardiogenic shock[12].

CONCLUSION

Acute yellow phosphorus poisoning can resultin impairment of liver function test which is comparably highly altered during first stage of intoxication and subsequently better during second and third stage and that could be due to supportive treatment. The statistical significance between liver parameters and the outcome on different occasions shows that the liver function parameters are better with say 3 and day 5, early initiation of treatment in turn helps in reducing the mortality due to yellow phosphorous poisoning. Also with treatment, fatal acute liver failure and multi-organ dysfunctioncan be prevented. Apart from the treatment and medications, easy access to poisoning agents should be restricted and periodic health education needs to be implemented in order to reduce

REFERENCES

1. McCarron MM, Gaddis GP and Trotter AT, 1981. Acute yellow phosphorus poisoning from pesticide pastes. Clinical Toxicology 18: 693-711.
2. Brent J, Wallace K and Buckhart K, 2005. Phosphorus. In: Critical care toxicology: diagnosis and management of the critically poisoned patient, eds Brent J, Wallace K, Buckhart K. pp 851-61. Elsevier Saunders.
3. Xie WG, Huang WW, Yao SG, Wang DY, Wang MX, Zhu ZQ et al., 2008. Rescue and treatment for mass burn casualties of yellow phosphorus explosion. Zhonghua Shao Shang ZaZhi. 24: 36-8.
4. Brent J, Wallace K, Buckhart K. Phosphorus. In: Brent J, Wallace K, Buckhart K, eds. Critical care toxicology: diagnosis and man- agement of the critically poisoned patient. Elsevier Saunders 2005:851-861.
5. Agency for Toxic Substances and Disease Registry (ATSDR). US Department of Health and Human Services, Public Health Ser- vice. Toxicological profile for white phosphorus. 1997. http:// www.atsdr.cdc.gov/tfacts103.html(accessed September 12, 2015).
6. Fernandez OU, CanizaresLL.Acutehepatotoxicityfrominges- tionof yellow phosphorus-containing fireworks. J ClinGastroenterol 1995; 21:139-142.
7. Chretien TE. Acute phosphorus poisoning: Report of a case with recovery.NEnglJMed1945;223:247-29.
8. Warnet JM, Claude JR, Truhaut R: Experimental biological toxicity of white phosphorus. Eur J ToxicologicHyg Environ 1973;6:57-64.
9. Mozingo DW Smith AA, McManus WF,et al: Chemcal burns. J Trauma 1988;28:642-647.
10. Klaser AE, Scalzo AJ, Blume C, et al. Ann Emerg Med 1996;28:713-718.
11. Brent J, Wallace KL, Burkhart KK, authors; Brent J, Wallace KL, Burkhart KK, Phillips SD, Donovan JW, editors. Phosphorus. Critical Care Toxicology – Diagnosis and Management of the Critically Poisoned Patient. 2005. Philadelphia, PA: Elsevier Mosby; p. 851–61
12. Talley RC, Linhart JW, Trevino AJ, authors. Acute elemental phosphorus poisoning in man: Cardiovascular toxicity. Am Heart J. 1972;84:139–40.